DOCKET NO.: ISIS-2508

PATENT

said DNA includes at least one nucleotide having a 2'-deoxy-erythro-pentofuranosyl sugar moiety covalently bound to one of said nucleobases; and

each of said PNAs [include] <u>includes</u> at least one peptide nucleic acid subunit having a covalently bound nucleobase.

19. (amended) A method of enhancing polynucleotide hybridization [and RNase H activation] in a organism, comprising contacting the organism with a macromolecule [of claim 1,] of the structure:

## PNA-DNA-PNA

wherein:

said DNA comprises at least one 2'-deoxynucleotide;

each of said PNAs comprise at least one peptide nucleic acid subunit;

said macromolecule has a sequence of nucleobases capable of specifically hybridizing to a complementary strand of nucleic acid; and

some of said nucleobases are located on the PNA portions of said macromolecule and some of said nucleobases are located on the DNA portion of said macromolecule.

20. (amended) A method of treating an organism having a disease characterized by the undesired production of a protein, comprising contacting the organism with a compound of [claim 1.] the structure:

#### PNA-DNA-PNA

# **DOCKET NO.: ISIS-2508**

**PATENT** 

wherein:

said DNA comprises at least one 2'-deoxynucleotide; and

each of said PNAs comprise at least one peptide nucleic acid subunit.

--24. The method of claim 20 wherein said each of said PNAs comprises a compound of the formula IIIa, IIIb or IIIc:

$$\begin{array}{c|c}
 & \downarrow \\
 & \downarrow \\$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^3 & N & O \\
 & C & H_2 \\
 & R^3 & N & O
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^3 & N & O \\
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & C & H_2 \\
 & R^7 & P
\end{array}$$

$$\begin{array}{c|c}
 & R^7 & P
\end{array}$$

## **DOCKET NO.: ISIS-2508**

## **PATENT**

$$\begin{array}{c|c}
 & C & H_2 \\
 & N & R^3 \\
 & O & N & R^3 \\
 & O$$

wherein:

B5

each L is independently selected from the group consisting of hydrogen, phenyl, heterocyclic moieties, naturally occurring nucleobases, and non-naturally occurring nucleobases;

each R<sup>7</sup> is independently selected from the group consisting of hydrogen and the side chains of naturally occurring alpha amino acids;

n is an integer from 1 to 60;

each of k, l, and m is independently zero or an integer from 1 to 5;

p is zero or 1;

Rh is OH, NH2 or -NHLysNH2; and

Ri is H or COCH<sub>3</sub>.

25. The method of claim 24 where each of said PNAs comprise a compound having formula (IIIa)-(IIIc) wherein each L is independently selected from the group consisting of the nucleobases thymine (T), adenine (A), cytosine (C), guanine (G) and uracil (U), k and m are zero or 1, and n is an integer from 1 to 30, in particular from 4 to 20.